Particularities of Diagnosis and Risk Assessment in the Young.

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Introduction (1)

- **In past**, hypertension affects older people.

➔ **These days**, high blood pressure affects people of all ages including young children.

- **Children** have **the same tests** for hypertension of adults; however, interpreting the numbers is **trickier**. → Consider child's **age, sex, and height**

Introduction (2)

- **The hypertension in young people** is an increasing problem in the world.

CARDIA

Coronary Artery Risk Development in Young Adults

Project Period: 12/30/1983–6/30/2018
Contact: Dr. Jared Reis

- **The CARDIA (**Coronary Artery Risk Development in Young Adults**) study** : elevated blood pressure in children is a predictor of the development of hypertension, and correlates with the presence of coronary artery calcification.

Adolescence Risk Factors Are Predictive of Coronary Artery Calcification at Middle Age

The Cardiovascular Risk in Young Finns Study

Objectives The purpose of this study was to examine the roles of adolescence risk factors in predicting coronary artery calcium (CAC).

Background Elevated coronary heart disease risk factor levels in adolescence may predict subsequent CAC independently of change in risk factor levels from adolescence to adulthood.

Methods CAC was assessed in 589 subjects 40 to 46 years of age from the Cardiovascular Risk in Young Finns Study. Risk factor levels were measured in 1980 (12 to 18 years) and in 2007.

Results The prevalence of any CAC was 19.2% (27.9% in men and 12.2% in women). Age, levels of systolic blood pressure (BP), total cholesterol, and low-density lipoprotein cholesterol (LDL-C) in adolescence, as well as systolic BP, total cholesterol, diastolic BP, and pack-years of smoking in adulthood were higher among subjects with CAC than those without CAC. Adolescence LDL-C and systolic BP levels predicted CAC in adulthood independently of 27-year changes in these risk factors. The multivariable odds ratios were 1.34 (95% confidence interval: 1.05 to 1.70; $p = 0.02$) and 1.38 (95% confidence interval: 1.08 to 1.77; $p = 0.01$), for 1-SD increase in adolescence LDL-C and systolic BP, respectively. Exposure to both of these risk factors in adolescence (defined as values at or above the age- and sex-specific 75th percentile) substantially increased the risk of CAC (multivariable odds ratio: 3.5 [95% confidence interval: 1.7 to 7.2; $p = 0.007$]) between groups with no versus both risk factors.

Conclusions Elevated adolescence LDL-C and systolic BP levels are independent predictors of adulthood CAC, indicating that adolescence risk factor levels play an important role in the pathogenesis of coronary heart disease.

(J Am Coll Cardiol 2012;60:1364–70)

Diagnosis
1. Blood Pressure Measurement

Blood Pressure in Children and Adolescents

- Normal range of blood pressure determined by body size and age
- Blood pressure standards developed based on **age, gender and height** of healthy population
- Blood pressure measurement preferred in the **right upper extremity**

  : because of the possibility of coarctation of the aorta, which might lead to false (low) readings in the left arm.

The 4th report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. USA

Blood Pressure Measurement

- **Children >3 years old** who are seen in a medical setting should have their BP measured.
- The preferred method of BP measurement is **auscultation**.
- Elevated BP must be confirmed on repeated visits before characterizing a child as having hypertension.
- Measures obtained by **oscillometric devices** that exceed the 90th percentile should be repeated **by auscultation**.

The 4th report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. USA

Blood pressure measurement

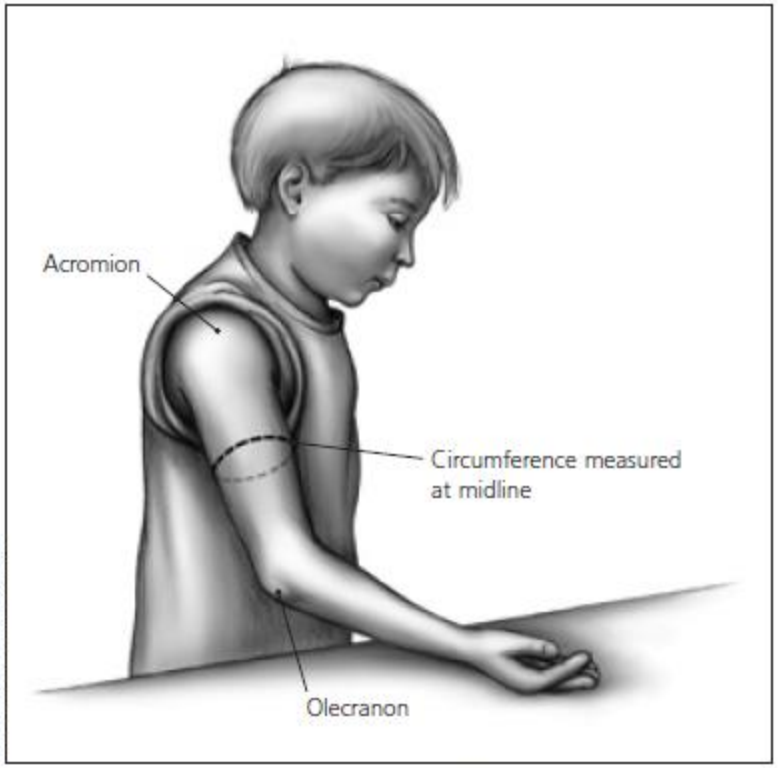

Figure 1. Arm circumference should be measured midway between the olecranon and acromial process.

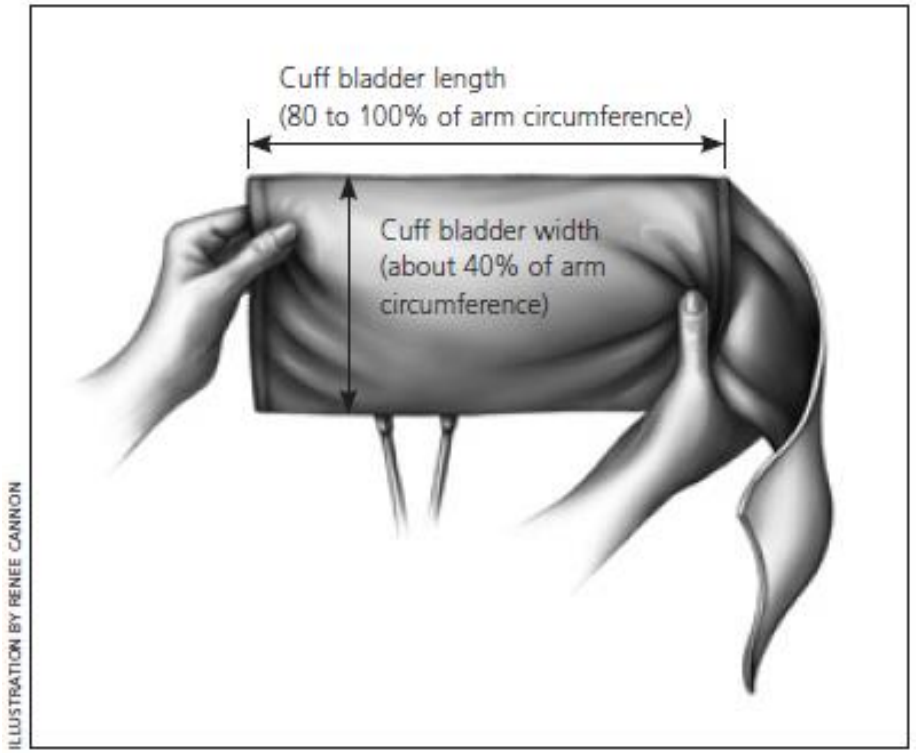

Figure 2. Blood pressure cuff showing size estimation based on arm circumference.

Recommended Dimensions for Blood Pressure Cuff Bladders

Age Range	Width (cm)	Length (cm)	Maximum Arm Circumference (cm)*
Newborn	4	8	10
Infant	6	12	15
Child	9	18	22
Small adult	10	24	26
Adult	13	30	34
Large adult	16	38	44
Thigh	20	42	52

* Calculated so that the largest arm would still allow bladder to encircle arm by at least 80 percent.

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Definitions of Hypertension

- **"Normal Blood Pressure":** < 90th percentile for age, gender and height.

- **"Pre-hypertension":** SBP and/or DBP >90th percentile but less than 95th percentile for age, gender and height.

  For age >12years, BP >120/80 regardless of 90th percentile considered pre-hypertension

The 4th report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. USA

Definitions of Hypertension

- **"Hypertension":** SBP and/or DBP >95th percentile for age, gender and height

  Stage 1: 95th – 99th percentile + 5 mmHg

  Stage 2: > 99th percentile + 5 mmHg

Confirmed on 3 or more occasions

The 4th report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. USA

Definitions of Hypertension

- **"White Coat Hypertension":** Blood pressure > 95th percentile in the physician's office, normotensive in outside environment

- **"Masked Hypertension":** Normal blood pressures in the physician's office, but high at home

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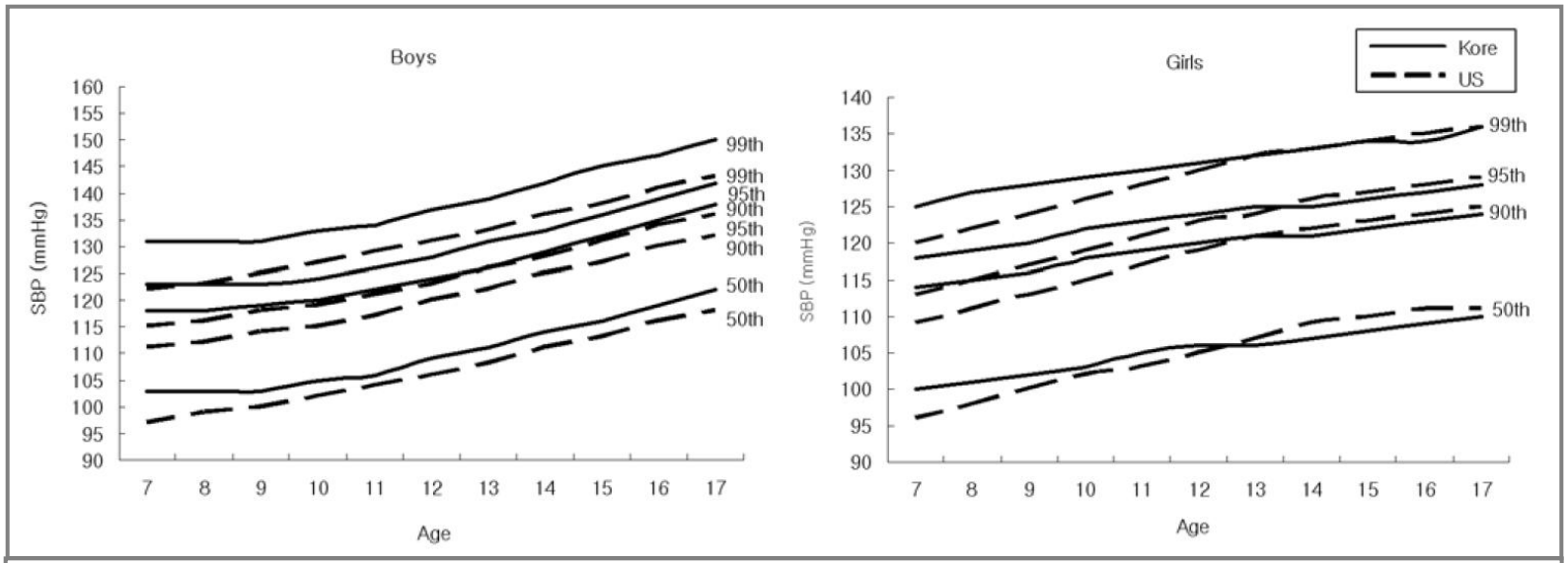
Blood Pressure Tables

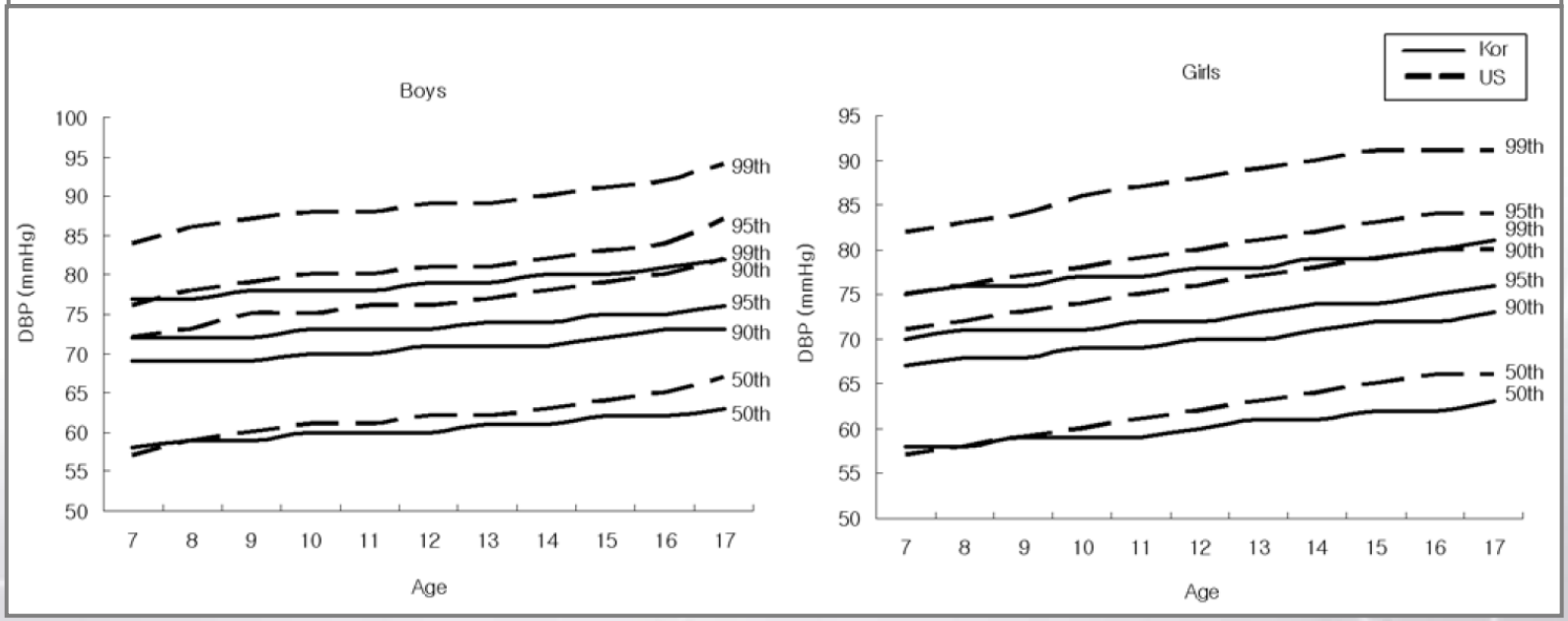
Boys

		SBP, mmHg							DBP, mmHg						
		Percentile Height							Percentile Height						
(Year)	Percentile	5th	10th	25th	50th	75th	90th	95th	5th	10th	25th	50th	75th	90th	95th
12	50th	102	103	104	105	107	108	109	61	61	61	62	63	64	64
	90th	116	116	117	119	120	121	122	75	75	75	76	77	78	78
	95th	119	120	121	123	124	125	126	79	79	79	80	81	82	82
	99th	127	127	128	130	131	132	133	86	86	87	88	88	89	90

The 4th report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. USA

한국 소아 청소년 정상 혈압 참고치





Korean J Pediatr 2008;51:33-41

Criteria for hypertension in children with respect to age and gender (2014 JSH)

	Systolic blood pressure (mm Hg)	*Diastolic blood pressure (mm Hg)*
Pre-school children	⩾120	⩾70
Elementary school		
First to third graders	⩾130	⩾80
Fourth to sixth graders	⩾135	⩾80
Junior high-school		
Boys	⩾140	⩾85
Girls	⩾135	⩾80
High-school	⩾140	⩾85

Classification of Hypertension in Children and Adolescents, With Measurement Frequency

	SBP or DBP Percentile	Frequency of BP Measurement
Normal	<90th	Recheck at next scheduled physical examination
Pre-HTN	90th to <95th or if BP exceeds 120/80 mmHg even if below 90th percentile up to <95th percentile	Recheck in **6 months**
Stage 1 HTN	95th percentile to the 99th percentile + 5 mmHg	Recheck in **1–2 wks** or **sooner** if the Pt. is symptomatic; **if persistently elevated on two additional occasions**, evaluate or refer to source of care **Within 1 month**.
Stage 2 HTN	>99th percentile + 5 mmHg	Evaluate or refer to source of care **within 1 week** or **immediately** if the patient is symptomatic.

The 4th report of HBP in children and adolescents. USA

Etiology of Hypertension

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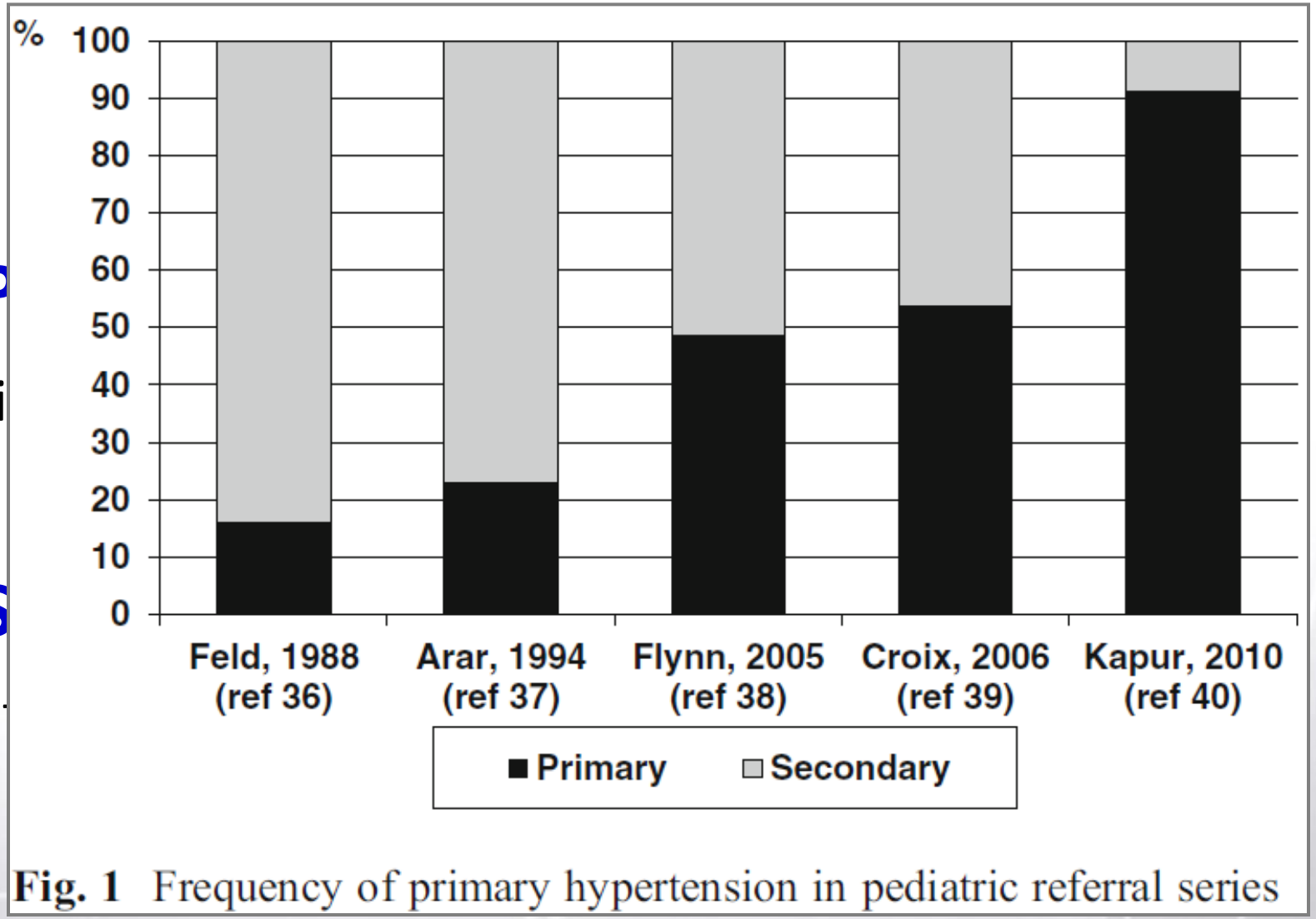


Fig. 1 Frequency of primary hypertension in pediatric referral series

Primary Hypertension

- More commonly found **in late childhood and adolescence**

  : Usually characterized by mild or stage 1 Hypertension

  : Associated with **overweight/obesity**

- Often associated with **F/Hx of HTN and cardiovascular disease**

Secondary HTN in Children

- More common in children than adults

  : **Children < 6 years old** >> 6-12 years old

  & adolescence (12-17 years old)

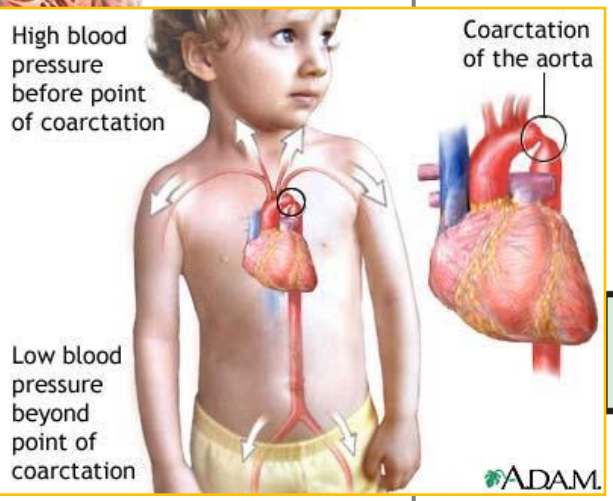
  : **Non-obese younger** children with high BP
- Consider this possibility in every child with HTN
- Majority of children with secondary hypertension will have **renal or renovascular disease**
- Thorough **history and physical exam** will likely give clues to underlying problems

2. Evaluation of secondary HTN

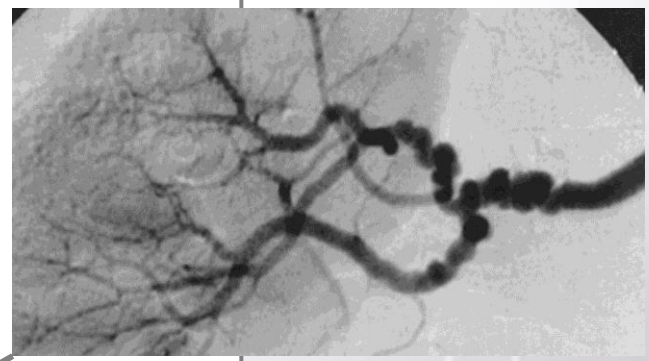
Most Common Causes of Secondary HTN by Age

Age groups	*Percentage of hypertension with an underlying cause*	*Most common etiologies†*
Children (birth to 12 years)	70 to 85	Renal parenchymal disease Coarctation of the aorta
Adolescents (12 to 18 years)	10 to 15	Renal parenchymal disease Coarctation of the aorta
Young adults (19 to 39 years)	5	Thyroid dysfunction Fibromuscular dysplasia Renal parenchymal disease
Middle-aged adults (40 to 64 years)	8 to 12	Aldosteronism Thyroid dysfunction Obstructive sleep apnea Cushing syndrome Pheochromocytoma
Older adults (65 years and older)	17	Atherosclerotic renal artery stenosis Renal failure Hypothyroidism

Am Fam Physician. 2010;82:1471-8.



- Documented hypertension
  - Gradient between upper and lower blood pressures
    - Yes → Coarctation of aorta
    - No → Abnormal urinalysis
      - Yes
        - Predominant white blood cells
          - Reflux nephritis
          - Recurrent urinary tract infections
          - Renal anomaly (and infection)
        - Predominant red blood cells
          - Postinfectious nephritis
          - Lupus nephritis
          - Henoch Schönlein purpura
          - Nephrocalcinosis
          - Nephrolithiasis
          - Other nephritis
          - Renal vein thrombosis
          - Thromboembolism
          - Tumor
      - No
        - Endocrine
        - Renovascular lesion
        - Essential hypertension



19th Edition, Nelson Textbook of Pediatrics

Signs and Symptoms That Suggest Specific Causes of Secondary Hypertension

Signs/symptoms	*Possible secondary hypertension cause*	*Diagnostic test options*
Apneic events during sleep Daytime sleepiness Snoring	Obstructive sleep apnea	Polysomnography (sleep study) Sleep Apnea Clinical Score with nighttime pulse oximetry
Flushing Headaches Labile blood pressures Orthostatic hypotension Palpitations Sweating Syncope	Pheochromocytoma	24-hour urinary fractionated metanephrines Plasma free metanephrines
Buffalo hump Central obesity Moon facies Striae	Cushing syndrome	24-hour urinary cortisol Late-night salivary cortisol Low-dose dexamethasone suppression
Hypokalemia	Aldosteronism	Renin and aldosterone levels to calculate aldosterone/renin ratio

Risk and Target organ Damage Assessment

Evaluation of HTN in Children and Adolescents

Must begin with:

-thorough **history** (including hx. of sleep disorder), **physical examination**

-**laboratory evaluation**

-**assessment of cardiovascular risk factors**:

- **overweight**
- **low plasma HDL cholesterol or high plasma triglycerides**
- **abnormal glucose tolerance**
- **F/Hx of HTN or CVD**

Laboratory evaluation of HTN

Basic:

- Serum chemistries, BUN, Cr, (PRA, Aldosterone level)
- CBC
- Urinalysis & Urine Culture
- Renal ultrasound with doppler

Evaluation for comorbidity:

- Fasting Lipid profile
- Fasting glucose
- Drug screen (if hx of drug use)
- Polysomnography (if hx of sleep disorder)

Evaluation for Target Organ Damage:

- Echocardiogram
- Retinal exam

Laboratory Testing for Children and Adolescents with Confirmed Prehypertension or Hypertension

Target population	*Recommended tests*	*Purpose*
All children with confirmed hypertension	Blood urea nitrogen and creatinine levels Complete blood count Electrolyte levels Renal ultrasonography Urinalysis Urine culture	Rule out underlying renal disease
All children with confirmed hypertension Overweight children with prehypertension	Fasting glucose level Fasting lipid panel	Rule out diabetes mellitus or hyperlipidemia as comorbid risk factors for cardiovascular disease
All children with confirmed hypertension Children with prehypertension and diabetes or renal disease	Echocardiography Retinal examination	Identify target organ damage, including left ventricular hypertrophy and pathologic vascular changes
Children with prehypertension or hypertension and a history suggestive of sleep disorder	Polysomnography	Rule out obstructive sleep apnea
Children with prehypertension or hypertension and a history suggestive of substance use	Drug screen	Rule out underlying substances contributing to or causing elevated blood pressure

NOTE: *Further studies may be indicated if there is a high degree of suspicion for secondary hypertension.*

Am Fam Physician. 2012;85:693-700

Additional Evaluation

- 24hr ABPM
- Renovascular imaging
  - -Renal scan
  - -Duplex Doppler flow studies
  - -MRA, CTA
  - -Arteriogram
- Other labs
  - -Plasma and urine metanephrines
  - -Plasma and urine steroids

Indications for routine performance of ABPM

- To confirm the diagnosis of sustained HTN or **WCH**
- To evaluate for the presence of **Masked HTN**
  : clinical suspicion of HTN but normal or preHTN casual measurements
- To assess **BP patterns in high-risk patients**
  : Assess for **abnormal circadian variation in BP**, such as blunted dipping or isolated sleep hypertension in patients with **DM, CKD**, solid organ transplants, and severe obesity w/wo sleep-disordered breathing.
  : Assess the **severity and persistence of BP elevation** in patients at high risk for **hypertensive TOD**
- **To evaluate effectiveness of drug therapy for hypertension**
  : Confirm BP control in treated patients - especially 2ndary HTN
  : Evaluate for apparent drug-resistant HTN or drug related Hypotension.

Target-Organ Abnormalities in Childhood Hypertension

- Target-organ abnormalities are commonly associated with HTN in children and adolescents.
- **Left ventricular hypertrophy (LVH)** is the most prominent evidence of target-organ damage.
- LVH reported (51 g/m2.7) in 34-38% of children with mild, untreated HTN with high correlation to BP and in particular ABPM. → Indication of anti-HTN Tx.
- Pediatric patients with established HTN should have echocardiographic assessment of left ventricular mass at diagnosis and periodically thereafter.

Left Ventricular Geometry and Severe Left Ventricular Hypertrophy in Children and Adolescents With Essential Hypertension

Stephen R. Daniels, MD, PhD; Jennifer M.H. Loggie, MD;
Philip Khoury, MS; Thomas R. Kimball, MD

Background—Left ventricular (LV) hypertrophy has been established as an independent risk factor for cardiovascular disease in adults. Recent research has refined this relationship by determining a cutpoint of 51 $g/m^{2.7}$ for LV mass index indicative of increased risk and defining LV geometric patterns that are associated with increased risk. The purpose of this study was to evaluate severe LV hypertrophy and LV geometry in children and adolescents with essential hypertension.

Methods and Results—A cross-sectional study of young patients (n=130) with persistent blood pressure elevation above the 90th percentile was conducted. Nineteen patients (14%) had LV mass greater than the 99th percentile; 11 of these were also above the adult cutpoint of 51 $g/m^{2.7}$. Males, subjects with greater body mass index, and those who had lower heart rate at maximum exercise were at significantly ($P<.05$) higher risk of severe LV hypertrophy. In addition, 22 patients (17%) had concentric LV hypertrophy, a geometric pattern that is associated with increased risk of cardiovascular disease in adults. Seven patients had LV mass index above the cutpoint and concentric hypertrophy. No consistent significant determinants of LV geometry were identified in these children and adolescents with hypertension.

Conclusions—Severe LV hypertrophy and abnormal LV geometry are relatively prevalent in young patients with essential hypertension. These findings suggest that these patients may be at risk for future cardiovascular disease and underscore the importance of recognition and treatment of blood pressure elevation in children and adolescents. Weight loss is an important component of therapy in young patients with essential hypertension who are overweight. **(*Circulation*. 1998;97:1907-1911.)**

Correlations between LV mass, Carotid IMT and Blood Pressure in in children with HTN

	LVM	Carotid IMT-SDS (cIMT-SDS)	Superficial femoral artery IMT-SDS (fIMT-SDS)
fIMT-SDS	p=0.02; r=0.291	p=0.0001; r=0.469	
Weight	p=0.0001; r=0.426		
BMI-SDS	p=0.001; r=0.402		
SBP (24 h)	p=0.01; r= 0.300	p=0.01; r=0.305	p=0.02; r=0.264
24-h SBP load		p=0.001; r=0.377	
Pulse pressure (24 h)		p=0.01; r=0.292	
Heart rate (24 h)	p=0.001; r=−0.361	p=0.01; r=−0.285	
SBP (day)		p=0.007; r=0.328	
Pulse pressure (day)		p=0.04; r=0.254	
Heart rate (day)	p=0.004; r=−0.350	p=0.01; r=−0.292	p=0.03; r=−0.291
Heart rate (night)	p=0.012; r=−0.311		
Homocysteine	p=0.01; r=0.309		
Uric acid	p=0.01; r=0.286		
CRP			p=0.01; r=0.305
Apoprotein A 1			p=0.01; r=−0.293
Apoprotein B			p=0.04; r=0.258
Birth weight	p=0.03; r=0.365		
Sodium, daily intake			p=0.04; r=0.252 (for absolute fIMT values)

72 children with EH (mean age: 14.5 years; range: 5–18 years)
Vs. control groups (103 age matched, healthy children)

Pediatr Nephrol 2006;21: 811–819

Intima-Media Thickness and Pulse Wave Velocity in Hypertensive Adolescents

Table 6. Comparison of pulse wave velocities in hypertension group and control group

PWV	Hypertension group	Control group
RhbaPWV (cm/sec)	745.9±63.2*	690.6±56.0
LhbaPWV (cm/sec)	759.2±60.8*	702.6±51.5

*$p<0.05$ significantly different from control group.
RhbaPWV, Right heart brachial-ankle pulse wave velocity; LhbaPWV, Left heart brachial-ankle pulse wave velocity.

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properties such as cross-sectional compliance and distensibility of the carotid artery. The carotid IMT significantly correlated with brachial-ankle PWV. In conclusion, the measurement of carotid IMT and brachial-ankle PWV might be useful to predict the development of atherosclerosis in hypertensive adolescents.

Key Words : *Carotid Intima-Media Thickness (cIMT); Pulse Wave Velocity (PWV); Hypertension; Atherosclerosis; Adolescent*

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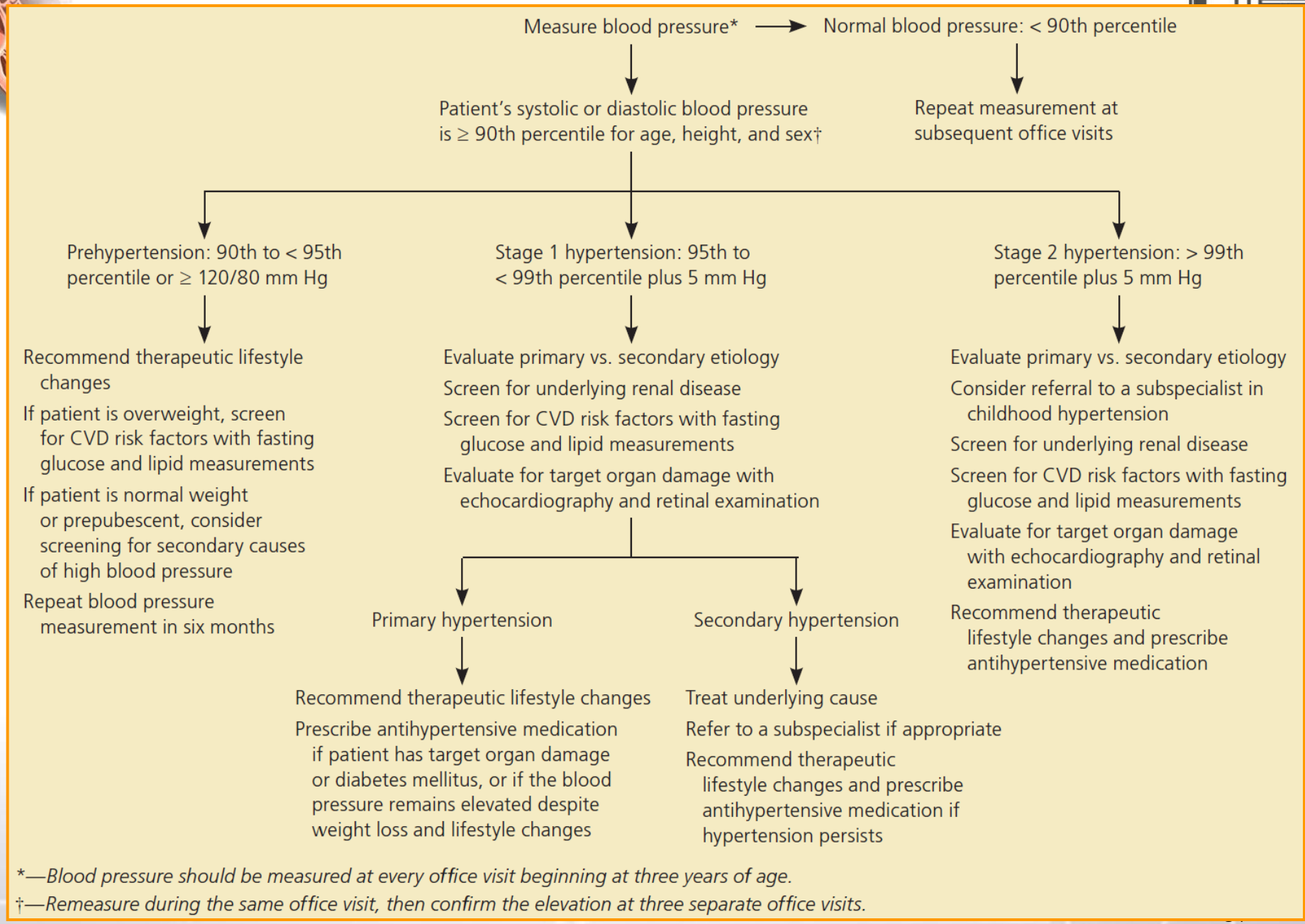
Summaries (1)

- Hypertension in children and adolescents is an early risk factor for cardiovascular (CV) morbidity and mortality.
- 1st Step : confirm that the blood pressure (BP) is truly elevated in accordance with the recommendation.
- In all cases, a careful history and physical examination are warranted.

Summaries (2)

- A family history for HTN or early cardiovascular events should be obtained.
- Evaluating for co-morbidities, and screening for evidence of 2ndary HTN and target organ damage.



*—Blood pressure should be measured at every office visit beginning at three years of age.

†—Remeasure during the same office visit, then confirm the elevation at three separate office visits.

Am Fam Physician. 2012;85:693-700

Thank you very much for your attention